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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,074	07/30/2003	David R. Milich	VACCINE-07971	9330

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EXAMINER	
BROWN, TIMOTHY M	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/630,074	MILICH ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-55* is/are pending in the application.

4a) Of the above claim(s) *55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *See infra*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication mailed August 10, 2003. The status of the claims is as follows:

Claims 1-24 have been canceled.

Claims 25-54 are under examination.

Claim 55 is withdrawn for comprising a non-elected invention.

Election/Restrictions

Applicant's election without traverse of Group VIII, claims 25-30 is acknowledged. Claim 55 is withdrawn for being drawn to a non-elected invention. Claim 55, drawn to a composition, is related to Group VIII as product and process of making. Thus, the inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). Because a polypeptide can be made using solid phase protein synthesis, the product of claim 55 can be made by a materially different process than the method of Group VIII. Restriction between Group VIII and claim 55 is therefore proper.

Information Disclosure

The PTO 1449 forms mailed by Applicants on October 29, 2003, January 23, 2004 and September 1, 2004 have been considered. These forms have been initialed, signed, and attached to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Undue experimentation is defined by the following factors: the nature of the invention; the breadth of the claims; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

Here, the breadth of the claims provides that (i) the modified hepatitis core antigen ("core antigen") is capable of producing particles despite the insertion or substitution of one or more acidic amino acids, and (ii) the core antigen may be derived from *any* hepatitis virus.

Regarding the first limitation, the specification does not enable the claimed alterations. The state of the art at the time the application was filed recognized that heterologous hepatitis core proteins (i.e. carrier proteins) were capable of forming viral particles. However, these carrier proteins were not modified by the addition and/or substitution of acidic amino acids as provided in the claims. Also, modifying the core antigen by inserting amino acids has an unpredictable effect on antigenicity and the carrier proteins' ability to form particles. For example, changing the composition of a heterologous cytomegalovirus antigen/HBV nucleocapsid protein produced

different results for VLP assembly and antigenicity (Tarar, M.R. FEMS (December 1996) 16, 183-192. These results are consistent with the alterations made by Applicants which show varying degrees of particle formation (see e.g. Example 9). Thus, one skilled in the art would need specific directions on how to substitute and/or insert acidic amino acids that rescue the core antigen's antigenicity and ability to form particles. The specification, however, fails to provide these directions. Rather, the specification teaches the insertion points for the heterologous polypeptide, and the C-terminal modifications that allow the carrier protein to assemble into particles. The specification is silent on the claimed acidic amino acid alterations that protect particle assembly.

Regarding the second limitation, the specification does not enable a core antigen that comprises any hepatitis virus. As noted above, making a heterologous HBV capsid protein that is antigenic and capable of forming particles requires knowledge of the specific regions that can be modified. However, the specification fails to teach any insertion points besides those for HBV. There is no discussion of the core regions of other viruses, such as HCV, that would support the insertion of a heterologous antigen.

Based on the lack of direction and unpredictability discussed above, one skilled in the art would have to invest undue experimentation in order to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25, 27, 28, 30-33, 35-41, 43, 44 and 46-54 are rejected under 35 U.S.C. 102(b) as being anticpated by Birkett (US 6,231,864).

Claims 25, 27, 28, 30-33, 35-41, 43, 44 and 46-54 are drawn to a method for producing an immunogenic composition comprising expressing a polynucleotide that encodes (i) a heterologous antigen, and (ii) a hepatitis core antigen, wherein at least one of said antigens is altered by the insertion or substitution of at least one acidic amino acid, and wherein said polynucleotide is expressed under conditions suitable for producing particles. The claims further provide that (i) the acidic amino acid may comprise a glutamic acid residue or an aspartic acid residue, (ii) that the alteration is made at the N-terminus or the C-terminus of the heterologous antigen, and (iii) that the heterologous antigen has an isoelectric point in the range of 3.0 to 6.0.

Birkett discloses a method of producing a carrier protein, wherein the carrier protein comprises a hepatitis B core protein having an insert of 1 to 40 amino acids, and wherein the insert is derived from an antigenic protein of a pathogen (col. 4, lines 12-31; and col. 9, lines 41-46). Birkett also discloses altering the carrier protein by inserting or substituting glutamic and/or aspartic amino acid residues at the C-terminus of the core protein (col. 5, lines 28-35). Finally, Birkett discloses expressing the carrier protein under conditions that permit the formation of particles (e.g. Examples ! and 2). Based on this disclosure, Birkett anticipates the subject matter of claims 25, 27, 28, 30-33, 35-41, 43, 44 and 46-54.

It should be noted that Birkett discloses the claimed isoelectric points through inherency. That is, Birkett's carrier protein would have a similar isoelectric focusing properties as the claimed heterologous antigen. It should also be noted that the rejection of the claims under Birkett does not give patentable weight to the functional language "under conditions suitable for producing particles."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

tmb

James C. Housel 9/19/05

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

TMB 9/12/05